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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SAUNDERS, DAVID A	

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/037,296	DAHLBACK ET AL.	
	Examiner	Art Unit	
	David A Saunders, PhD	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-22,31 and 33-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *20-22,31 and 33-47* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The amendment of 4/22/04 has been entered. Claims 20-22, 31 and 33-47 are pending and under examination.

Claims 20 and 31 are objected to under 37 CFR 1.75 (c) for failing to indent each recited component of the kit or composition.

Claim 31 is objected to because of the following informalities: In claim 31, line 3 the Greek letter "beta" is missing before "chain". Appropriate correction is required.

Claim 43 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 43 merely states types of aqueous solutions that the kit of base claim 31 might be used with. Since these aqueous solutions are not themselves provided as a kit component, claim 43 does nothing to limit the nature of the components provided in the kit.

Claims 20-22, 31 and 33-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 20 and 31 are unclear by reciting "an amino acid sequence homologous or analogous to the extreme N-Terminal SCR – module". Applicant's disclosure has not defined the terms "homologous" and "analogous". One has no idea as to what structural similarities in sequence are required for one to consider a polypeptide as having a sequence that is "homologous" or "analogous". One has no idea as to what functional characteristic(s) must be retained and what functional characteristics may be

absent in a polypeptide that "homologous" or "analogous". Additionally applicant has not defined these terms so that one knows what the difference in scope/content would be for each.

Further confusion is added by the fact that one of skill would read the terms "homologous" or "analogous" as indicating that the ligand sequence of claims 20 and 31 is different from that of the extreme N-terminal SCR-module; however, dependent claims 37 and 44 require that the ligend be the extreme N-terminal SCR module.

In claims 31, line 5 "a fragment" thereof" is confusing. What does this modify – the "antibody" of line 4, or the "proteins" of line 5?

Claim 31 is confusing by claiming a "composition", which is a term implying that everything recited is present in one mixture. It is deemed that, if one wanted to sell the instant "composition", the "ligand" and reagent "capable of releasing protein S" should be packaged separately.

Claims 34 and 46 has an improper Markush Group. The "matrix" member is not clearly different in scope from the "carrier" of claim 21. Applicant's disclosure has used the terms "solid carrier" and "solid matrix interchangeably; thus the member recited as "matrix" fails to further define the "solid carrier in any manner.

Claims 20-22, 33-43 and 46-47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time

the application was filed, had possession of the claimed invention. The claims contain new matter.

In claim 20, line 5 " a fragment thereof" is new matter, if this modifies "Protein S" since applicant has not disclosed in kit containing both the "extreme N-terminal SCR-module of the B-chain" and a "fragment" of Protein S. Examiner finds no disclosed use of a protein S fragment in an assay for free Protein S; the only disclosed use of fragments of Protein S is for the raising of antibodies for free protein S. (page 5, lines 24-31).

In claims 33-34 and 46-47 "a bead" lacks support. The only original recitation of "beads" is at page 13, line 29, wherein the beads are specifically disclosed as being "of polystyrene" and "having a diameter of about 5 mm." Applicant has improperly broadened the scope of the nature of the bead.

In claims 34 and 46 "gel" lacks support. Examiner finds no "gel" taught in the para. spanning pages 13-14.

In claims 34 and 46 "sheet" lacks support, except for those that are "nitrocellulose – or nylon-based webs." See page 13, line 31. Applicant has improperly broadened the nature of the "sheets".

In claim 43, "blood, plasma or serum" lack disclosure support. At page 6, lines 27+ the examiner finds no teaching of these as the fluid sample to be purified. Applicant has improperly recited undisclosed species.

Regarding the prior art rejections of record it is to be noted that claim 20 is confusing and can be read in alternative ways with respect to the nature of the reagents

(112, 2nd above); also it is to be noted (infra) that applicant's urgings regarding the nature of the claimed invention lead to confusion. Therefore the examiner has no choice but to maintain rejection(s) as follows:

Claims 20-22, 33-40 and 42 are rejected under 35 U.S.C. 102(a) as being anticipated by Griffin et al (WO 93/01209).

As previously noted Griffin et al generally describe kits for detecting free Protein – S (PS) at pages 36-42 and describe a competition assay at pages 50-52. The competition assay uses purified C4BP affixed to a solid phase (page 51, lines 3 and 15) and uses a PS fragment operatively linked to an indicating means (page 51, lines 7-15). These correspond, respectively, to the instant "ligand" (line 2) and "fragment" (line 5); their provision in a kit would anticipate instant claims 20-21 and 37.

The examiner notes that claim 20 and 37 encompass the full length purified C4BP of Griffin et al; by virtue of reciting "comprising" more than just "the extreme N-terminal SCR-module" can be present.

The examiner also notes that, at first blush claim 20 does not appear to be anticipated, because it requires a ligand having a sequence" homologous" or "analogous" to the nature sequence of C4BP that would be present in the purified C4BP of Griffin et al. However it is noted that dependent claim 37 states that the ligand "comprises the extreme N-terminal SCR-module of the B-Chain of the C4BP molecule"; this literally encompasses the native sequence. On the principle that what is recited in dependent claim 37 would necessarily be encompassed by independent claim 20, claim

20 is rejected. Examiner also notes applicant has not urged that "homologous" or "analogous" distinguish.

Examiner further notes that claim 20, line 4 requires that the reagent be "other than protein S". Since the PS fragments of Griffin et al (page 51, line 14) are not "Protein S" per se, they are properly considered to be "other than protein S." Examiner also notes that the labeled PS fragment of Griffin et al anticipates instant "fragment thereof" assuming this modifies "Protein S" immediately proceeding.

The examiner notes that applicant considered amended claim 20 distinguishes from Griffin et al because Griffin et al teach a competitive binding assay, while the instant assay requires "an indicating means capable of producing a detectable signal indicative of the formation of a complex between free protein S and the ligand"; applicant does not consider that the competitive binding assay forms such a complex. This argument is faulty for the following reasons.

1) Applicant is arguing the nature of the assay steps and not the nature of what is provided in the kit. Following the rational stated supra, Griffin et al provide the ligand (purified C4BP) and reagent (labeled PS peptide) of the instant kit. How they may be used in the reference makes no difference.

2) Even if weight were given to recitation of "producing a detectable signal indicative of the formation of a complex..." it would not be necessary for Griffin et al to disclose any reagent with such an indicating means. Applicant is claiming a kit having a ligand and a reagent; the latter can be any one of an "antibody", a "fragment", or an

"indicating means". The rejection over Griffin et al is based upon the reagent being a "fragment" of Protein S.

3) Applicant is also in error in considering that "a detectable signal indicative of the formation of a complex between free Protein S and the ligand" rules out a competitive binding assay and the components therefore. Any format of binding assay, whether it directly measures the amount of ligand-binder complex (e.g. as in a sandwich assay), or whether it indirectly measures the amount of ligand binder complex (e.g. as in a competitive assay binding assay which gives a signal inversely related to the amount of complex) is "indiative of formation of a complex". Arguments that Griffin et al show a competivive assay and components therefore are not persuasive.

As noted above Griffin et al anticipate claims 20-21 and 37.

Regarding claims 22 and 33-34, note teachings of certain beads and micotitre plates as conventional solid carriers/ matrices at page 42, lines 9-20.

Regarding the indicating means of claims 38-39, note Griffin et al at page 38, line 23 pages 40, line 31.

For the "substrate" of claim 40, note that page 40, lines 1-2 teach substrates for an enzyme indicator.

From the above, instant claims 20-22, 33-34, 37-40 are anticipated by Griffin et al.

Because applicant has amended claim 20 to have multiple embodiments and because numerous dependent claims thereof were not rejected over the above

teachings of Griffin et al, the examiner can properly rely upon teachings of Griffin et al previously not considered.

Griffin et al teach an alternative format of competition assays (page 52, lines (3-13) that utilize solid phase immobilized C4BP (following rational stated supra, this is the ligand of claim 20) and labeled anti-PS. Sub. F antibody (this is the antibody specific for protein S). This assay thus uses the ligand and one of the reagent components recited in claim 20, and their packaging within a kit follows from Griffin et al. Even though this is a competition/assay, this still anticipates because.

1) applicant is claiming a kit with components, not an assay method using these components.

2) the antibody component of claim 20 is an alternative to the "indicating" means component of the kit.

3) a competition assay yields a detectable signal that is indicative (via an inverse relationship) of the extent of the formation of a ligand binder complex. See more complete explanation of points 1)-3) further supra.

From teachings related to this noted alternative embodiment of Griffin et al instant claims 20-21, 37 and 42 are anticipated.

Teachings regarding the "solid carriers" of claims 22 and 33-34 have been noted supra.

Teachings with respect to the "indicating means" of claims 38-40 have also been noted above.

Regarding claims 21-22, note Griffin et al at page 25, line 11 – page 36, line 26.

From these considerations claims 20-22, 33-40 and 42 are anticipated.

The 102 rejection over Griffin et al has thus been maintained for claims 20-22 and extended to new claims 33-40 and 42.

The 102 rejection over Harding et al has been withdrawn.

Claims 20-22, 33-40 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harding et al in view of Griffin et al.

Harding et al teach instant C4BP and various alpha/beta chain chimeras of C4BP that contain the extreme N-terminal SCR module immobilized on microtitre plates. Griffin et al teach that a microtitre plate with immobilized C4BP can be used to assay for free PS via two competitive binding formats (one using a labeled PS fragments, the other using a labeled anti-PS. sub. F antibody), and they teach that assay components can be packaged in kits. Provision of either the intact C4BP or chimeric form of Harding et al in kits for the assays taught by Griffin et al would have been obvious.

Applicant has traversed the rejection of record by arguing that there is no motivation to combine these references but has offered no scientific/legal rational as to why. The examiner previously offered motivation (action of 12/19/03, at page 4, last paragraph), and applicant has not argued that the reasoning is erroneous.

Applicant has urged that the combination of Harding et al and Griffin et al does not provide that reagent instantly defined in claim 20, that they only show labeled protein S as a competing regent. To the contrary, the examiner finds that Griffin et al teach a labeled fragment of protein –S (page 51, line 14); this corresponds to the "fragment thereof" of instant claim 20, assuming this modifies "protein S" preceeding.

Also to the contrary, Griffin et al teach a labeled antibody designated as anti-PS. sub. F (page 52, lines 5-7); this corresponds to the antibody of instant claim 20.

Other arguments concerning the operative made of competition reactions and the nature of the "indicating means" of the claim are not convincing for the same reasons set forth supra for anticipation over Griffin et al.

From the above, the rejection over Harding et a in view of Griffin et al is applied to claims 20-22 and extended to new claims 33-40 and 42; with reliance upon Griffin et al for teaching aspects of solid carriers, antibodies and indicators recited in the new claims.

Applicant's arguments filed on 4/22/04 have been fully considered but they are not persuasive for the reasons set forth above.

The amendment has overcome previously stated prior art rejections of claim 31. New claims 43-47 depending therefrom is not rejected over prior art.

The amendment has overcome the previously stated rejection of claim 20 over Hillarp et al.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Saunders whose telephone number is (571) 272-0849. The examiner can normally be reached on Monday to Thursday from 8 AM to 5:30 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David A Saunders

DAVID SAUNDERS
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Saunders/LR
July 12, 2004